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10/568,488	03/25/2008	Brett P. Monia	ISPH-0859USA	7913

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,488	MONIA ET AL.	
	Examiner	Art Unit	
	TERRA C. GIBBS	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34,42,43,48-53,58 and 68-82* is/are pending in the application.

4a) Of the above claim(s) *71-82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34,42,43,48-53,58 and 68-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *November 3, 2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission mailed on November 3, 2009 has been entered.

New claims 68-82 are acknowledged. Claims 34, 51, and 58 have been amended.

Claims 34, 42, 43, 48-53, 58 and 68-82 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Applicant's Amendment and Response filed November 3, 2009 have been considered. Rejections and/or objections not reiterated from the previous Office Action mailed June 9, 2009 are hereby withdrawn. Any arguments addressing said rejections and/or objections are moot. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Election/Restrictions

Claims 71-82 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on August 19, 2008.

However, Applicant is reminded that the Examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Accordingly, claims 34, 42, 43, 48-53, 58, and 68-70 have been examined on the merits.

Information Disclosure Statement

Applicant's information disclosure statement filed November 3, 2009 is acknowledged. The submission is in compliance with the provisions of 37 CFR §1.97. Accordingly, the Examiner has considered the information disclosure statement, and a signed copy is enclosed herewith.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 34, 42, 43, 48-53, 58, and 68-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,994,076 (of record), as evidenced by Branch, AD (TIBS, 1998 Vol.23:45-50), in view of U.S. Patent No. 6,906,186.

Claim 34 is drawn to an antisense compound comprising a modified oligonucleotide consisting of 13 to 30 linked nucleosides targeted to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase, wherein said modified oligonucleotide comprises at least one modified sugar moiety or at least one modified nucleobase, wherein said modified oligonucleotide is complementary to at least an 8 contiguous nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1, wherein said modified oligonucleotide specifically hybridizes to SEQ ID NO:1, and wherein the modified oligonucleotide does not comprise SEQ ID NO:91 or 92. Claims 42, 43, 48-53, 58, and 68-70 are dependent on claim 34 and include all the limitations of claim 34 with the further limitations wherein the antisense compound comprises a chimeric oligonucleotide; wherein the antisense compound is a single-stranded or a double-stranded compound; wherein the antisense compound comprises at least one phosphorothioate linkage; wherein the antisense compound comprises at least one 2'-O-methoxyethyl moiety; wherein the antisense compound comprises at least one 5-methyl cytosine; wherein the antisense compound comprises a pharmaceutical composition comprising a pharmaceutically acceptable carrier; and wherein the modified oligonucleotide comprises a gap segment consisting of linked deoxynucleosides.

Determining the scope and contents of the prior art

U.S. Patent No. 5,994,076 teaches SEQ ID NO:1090, which is a p38α mitogen-activated protein kinase antisense gene-specific primer. SEQ ID NO:1090 is 100% complementary to at least an 8 contiguous nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1 of Applicant's invention. See specifically nucleotides 1194 to 1203 of SEQ ID NO:1. Given this high degree of homology/similarity, the p38α mitogen-activated protein kinase antisense gene-specific primer taught by U.S. Patent No. 5,994,076 meets the structural limitations of the claimed invention and would be expected to specifically hybridize to SEQ ID NO:1, absent evidence to the contrary.

U.S. Patent No. 5,994,076 teaches that the gene specific primers may be modified in a variety of ways. U.S. Patent No. 5,994,076 teaches the gene specific primers are comprised in a buffer medium, which constitutes a pharmaceutically acceptable carrier.

It is noted that U.S. Patent No. 5,994,076 are silent as to whether or not SEQ ID NO:1090 also has antisense activity. However, since SEQ ID NO:1090 meets the structural limitations of the claimed invention and would be expected to specifically hybridize to SEQ ID NO:1, it is the Examiner's opinion that SEQ ID NO:1090 will act as an antisense oligonucleotide, absent evidence to the contrary. The burden of establishing whether SEQ ID NO:1090 taught by U.S. Patent No. 5,994,076 would have the additional function of acting as an antisense oligonucleotide under generally any assay conditions falls to Applicant. See MPEP 2112.01, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are

produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433." See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting *In re Best* 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that SEQ ID NO:1090 taught by U.S. Patent No. 5,994,076 would or would not have the additional function of being an antisense oligonucleotide as instantly claimed.

It is noted that the use of an oligonucleotide as an antisense oligonucleotide is an intended use limitation. If the prior art oligonucleotide is capable of forming a hybrid with an mRNA, it can function as an antisense oligonucleotide as evidenced by Branch.

For example, according to Branch, at page 47, third column, first paragraph:

In considering whether ODNs have the requisite power of discrimination, it is crucial to know their mechanism(s) of action. These mechanisms may differ from cell type to cell type and may depend upon the exact nature of the target RNA and the ODN. However, there is strong evidence that in several systems, including *Xenopus* oocytes[32] and permeabilized cells[33], the target RNA is destroyed by the action of RNase H. RNase H activities cleave the RNA component of DNA–RNA hybrids. They do not require long hybrid regions as substrates. In fact, *in vitro*, RNase H can cleave a hybrid containing only 4 bp (Ref. 34). In *Xenopus* oocytes, as few as 10 bp are sufficient[35]. For standard ODNs, it is likely that 10 bp are also sufficient in human cells; in the case of certain chemically modified nucleotides, it is proven that as few as 7 bp can lead to cleavage[36].

Ascertaining the differences between the prior art and the claims at issue

U.S. Patent No. 5,994,076 does not teach an antisense compound which comprises a chimeric oligonucleotide; wherein the antisense compound is a single-stranded or a double-stranded compound; wherein the antisense compound comprises at least one phosphorothioate linkage; wherein the antisense compound comprises at least one 2'-O-methoxyethyl moiety; wherein the antisense compound comprises at least one 5-methyl cytosine; wherein the antisense compound comprises a pharmaceutical composition; and wherein the modified oligonucleotide comprises a gap segment consisting of linked deoxynucleosides.

U.S. Patent No. 6,906,186 teaches antisense oligonucleotide compounds targeted to a protein kinase. U.S. Patent No. 6,906,186 teaches that the antisense

oligonucleotide compounds targeted to a protein kinase are modified, where modified oligonucleotides are often preferred over native forms because of desirable properties such as, enhanced cellular uptake, enhanced affinity for nucleic acid target and increased stability in the presence of nucleases. U.S. Patent No. 6,906,186 teaches antisense compounds comprising a chimeric oligonucleotide; wherein the antisense compound is a single-stranded or a double-stranded compound; wherein the antisense compound comprises at least one phosphorothioate linkage; wherein the antisense compound comprises at least one 2'-O-methoxyethyl moiety; wherein the antisense compound comprises at least one 5-methyl cytosine; wherein the antisense compound comprises a pharmaceutical composition; and wherein the modified oligonucleotide comprises a gap segment consisting of linked deoxynucleosides.

Resolving the level of ordinary skill in the pertinent art

The level of ordinary skill in the pertinent art is considered to be high, being a graduate student or post-doctoral fellow in a biological science.

Considering objective evidence present in the application indicating obviousness or nonobviousness

It would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made to make an antisense compound comprising a modified oligonucleotide consisting of 13 to 30 linked nucleosides targeted to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase, wherein said modified oligonucleotide comprises at least one modified sugar moiety or at least one modified nucleobase, wherein said modified oligonucleotide is complementary to at least an 8 contiguous nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1, wherein

said modified oligonucleotide specifically hybridizes to SEQ ID NO:1, and wherein the modified oligonucleotide does not comprise SEQ ID NO:91 or 92 since SEQ ID NO:1090 taught by U.S. Patent No. 5,994,076 meets the structural limitations of the claimed invention and would be expected to specifically hybridize to SEQ ID NO:1 and exhibit antisense activity, as evidenced by Branch, absent evidence to the contrary.

It would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made to have the antisense compound comprise modified sugar moieties or modified nucleobases using the teachings and motivation of U.S. Patent No. 6,906,186.

One of ordinary skill in the art would have been motivated to make an antisense compound comprising a modified oligonucleotide consisting of 13 to 30 linked nucleosides targeted to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase, wherein said modified oligonucleotide comprises at least one modified sugar moiety or at least one modified nucleobase, wherein said modified oligonucleotide is complementary to at least an 8 contiguous nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1, wherein said modified oligonucleotide specifically hybridizes to SEQ ID NO:1, and wherein the modified oligonucleotide does not comprise SEQ ID NO:91 or 92 since U.S. Patent No. 5,994,076 taught that such an oligonucleotide could specifically hybridize to a p38α mitogen-activated protein kinase.

One of ordinary skill in the art would have been motivated to have the antisense compound comprise modified sugar moieties or modified nucleobases since U.S. Patent No. 6,906,186 teaches that such modifications enhance stability and protect the

oligonucleotide from enzymatic nucleases.

One of ordinary skill in the art would have had a reasonable expectation of success of making an antisense compound comprising a modified oligonucleotide consisting of 13 to 30 linked nucleosides targeted to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase, wherein said modified oligonucleotide comprises at least one modified sugar moiety or at least one modified nucleobase, wherein said modified oligonucleotide is complementary to at least an 8 contiguous nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1, wherein said modified oligonucleotide specifically hybridizes to SEQ ID NO:1, and wherein the modified oligonucleotide does not comprise SEQ ID NO:91 or 92 since U.S. Patent No. 5,994,076 taught the successful use and design of such an oligonucleotide as an oligonucleotide that could specifically hybridize to a p38α mitogen-activated protein kinase. One of ordinary skill in the art would have had a reasonable expectation of success of making a composition comprising an antisense oligonucleotide that specifically hybridizes to a p38α mitogen-activated protein kinase since U.S. Patent No. 5,994,076 taught an oligonucleotide that specifically binds to a p38α mitogen-activated protein kinase and it is accepted in the art that if an oligonucleotide is capable of forming a hybrid with an mRNA, it can successfully function as an antisense oligonucleotide.

One of ordinary skill in the art would have had a reasonable expectation of success of having the antisense compound comprise modified sugar moieties or modified nucleobases since U.S. Patent No. 6,906,186 taught the successful use and

design of antisense compounds targeted to a protein kinase comprising modified oligonucleotides, including modified sugar moieties or modified nucleobases.

Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of filing.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached from 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tracy Vivlemore can be reached on 571-272-2914. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN

USA OR CANADA) or 571-272-1000.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

January 14, 2010
/Terra Cotta Gibbs/